



Complete Summary

GUIDELINE TITLE

The management of ovarian hyperstimulation syndrome.

BIBLIOGRAPHIC SOURCE(S)

Royal College of Obstetricians and Gynaecologists (RCOG). The management of ovarian hyperstimulation syndrome. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2006 Sep. 11 p. (Green-top guideline; no. 5). [34 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Royal College of Obstetricians and Gynaecologists (RCOG). Management and prevention of ovarian hyperstimulation syndrome. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2005 Jan.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [February 28, 2008, Heparin Sodium Injection](#): The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

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SCOPE

DISEASE/CONDITION(S)

Ovarian hyperstimulation syndrome

GUIDELINE CATEGORY

Diagnosis
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Family Practice
Obstetrics and Gynecology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide clinicians with up-to-date information about the diagnosis and treatment of ovarian hyperstimulation syndrome, based upon the best available evidence

TARGET POPULATION

Women with suspected or known ovarian hyperstimulation syndrome

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Risk Assessment

1. Assessment of symptoms and classification of disease severity
2. Clinical examination

- Assessment of pain, breathlessness, hydration, weight, cardiovascular function
 - Heart rate, blood pressure
 - Abdominal girth, distention, ascites
 - Fluid intake and output chart
3. Laboratory investigations
- Full blood count
 - Haemoglobin, haematocrit, white cell count
 - Urea and electrolytes
 - Liver function tests
 - Baseline clotting studies
 - Pelvic ultrasound (for ascites and ovarian size)
 - Chest s-ray or ultrasonography (if respiratory symptoms)
 - Electrocardiogram (ECG) and echocardiogram (if suspect pericardial effusion)

Management/Treatment

1. Provision of written information about ovarian hyperstimulation syndrome (OHSS) to women undergoing ovarian stimulation
2. Development of protocols for OHSS management and referral of women with suspected OHSS to hospital
3. Hospitalization, including intensive care for critical OHSS
4. Pain relief (paracetamol, oral or parenteral opiates)
5. Counselling and support
6. Monitoring (frequency of assessment)
7. Management of fluid balance (oral intake to thirst, diuretics with caution, as indicated)
8. Management of ascites (paracentesis under ultrasound guidance, intravenous colloid replacement)
9. Testing for thrombophilia in women with a personal or family history of thrombosis
10. Thromboprophylaxis (support stockings, heparin, pneumatic compression)
11. Pelvic surgery as indicated
12. Reporting of adverse outcomes

MAJOR OUTCOMES CONSIDERED

- Incidence of ovarian hyperstimulation syndrome (OHSS)
- Pregnancy outcome following OHSS, including miscarriage, hypertension, placental abruption, preterm delivery, low birth weight
- Complications of OHSS treatment
- Symptom relief
- Morbidity and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Original articles considered when writing this guideline were obtained following a literature search of Medline January 1966–April 2006 and Embase January 1980–April 2006 electronic databases using the keyword "ovarian hyperstimulation syndrome." This was complemented by hand searching from original references and reviews. Although the literature search revealed few comparative studies on best management, this guideline provides information to assist clinical management, linking recommendations to both the evidence and reasoning of the guidelines development group. The definitions of the types of evidence used in this guideline originate from the US Agency for Health Care Policy and Research. No systematic reviews or meta-analyses were identified from the literature search.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia: Evidence obtained from meta-analyses of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well-designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study

III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The recommendations were graded according to the level of evidence upon which they were based. The grading scheme used was based on a scheme formulated by the Clinical Outcomes Group of the National Health Service Executive.

Grade A - Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)

Grade B - Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)

Grade C - Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Following discussion in the Guidelines and Audit Committee, each green-top guideline is formally peer reviewed. At the same time the draft guideline is published on the Royal College of Obstetricians and Gynaecologists Web site for further peer review discussion before final publication.

The names of author(s) and nominated peer reviewers are included in the original guideline document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the original guideline document.

Levels of evidence (**Ia-IV**) and grading of recommendations (**A-C**) are defined at the end of the "Major Recommendations" field.

Incidence of Ovarian Hyperstimulation Syndrome (OHSS)

What Is The Reported Incidence of OHSS?

B - Women should be informed that mild forms of OHSS are common, affecting up to 33% of *in vitro* fertilisation (IVF) cycles and that 3 to 8% of IVF cycles are complicated by moderate or severe OHSS.

Diagnosis of OHSS

A diagnosis of OHSS is usually straightforward, given a history of ovarian stimulation, either by gonadotrophins or antiestrogens, followed by the typical symptoms of abdominal distension, abdominal pain, nausea, and vomiting. Nevertheless, alternative diagnoses should always be considered, such as a complication of an ovarian cyst (torsion, haemorrhage), pelvic infection, intra-abdominal haemorrhage, ectopic pregnancy, and appendicitis.

Assessing Severity and Reporting Adverse Outcomes

How Is The Severity of OHSS Classified and Reported?

C - In the United Kingdom (UK), any death related to OHSS must be reported to the Confidential Enquiries into Maternal Deaths, irrespective of whether the woman was pregnant. Units should follow relevant Human Fertilisation and Embryology Authority (HFEA) guidelines for reporting severe untoward incidents.

A classification of the severity of OHSS is in the table below.

Table. Classification of Severity of OHSS

Grade	Symptoms
Mild OHSS	<ul style="list-style-type: none">• Abdominal bloating• Mild abdominal pain• Ovarian size usually <8 cm*
Moderate OHSS	<ul style="list-style-type: none">• Moderate abdominal pain• Nausea \pm vomiting• Ultrasound evidence of ascites

Grade	Symptoms
	<ul style="list-style-type: none"> • Ovarian size usually 8–12 cm*
Severe OHSS	<ul style="list-style-type: none"> • Clinical ascites (occasionally hydrothorax) • Oliguria • Haemoconcentration haematocrit >45% • Hypoproteinaemia • Ovarian size usually >12 cm*
Critical OHSS	<ul style="list-style-type: none"> • Tense ascites or large hydrothorax • Haematocrit >55% • White cell count >25,000/mL • Oligo/anuria • Thromboembolism • Acute respiratory distress syndrome

*Ovarian size may not correlate with severity of OHSS in cases of assisted reproduction because of the effect of follicular aspiration.

Women at Risk of OHSS

What Advice Should Women Receive About the Risk of OHSS?

C - Assisted conception units should provide women with written information about OHSS including risks, symptoms of OHSS, what action to take, and a 24-hour contact number with prompt access to a clinician with the necessary expertise in the diagnosis and management of OHSS. Women should be advised to keep this information with them at all times and show it if they seek medical help.

All women undergoing ovarian stimulation should be considered at risk of OHSS and should be provided with clear face-to-face advice about the condition, backed up by written information. Women at higher risk of developing OHSS include those with polycystic ovaries, women under 30 years of age, use of gonadotrophin-releasing hormone (GnRH) agonists, development of multiple follicles during treatment, exposure to luteinizing hormone/human chorionic gonadotrophin (LH/hCG), and previous episodes of OHSS. (Evidence level IV)

Outpatient Management

How Should the Treatment for Women With Suspected OHSS Be Managed?

C - Units carrying out treatment that has a potential for resulting in OHSS should develop agreed protocols for referral of women with suspected OHSS to hospital care, including written protocols for initial OHSS management. Protocols should be available to referring practitioners, neighbouring gynaecology departments, and accident and emergency departments in their catchment areas.

Assessment of the woman will usually involve clinical examination, which should include body weight and abdominal girth measurement, and pelvic ultrasound examination to measure ovarian size and check for ascites. Laboratory investigations that are helpful in assessing the severity of OHSS are haemoglobin, haematocrit, serum creatinine, and electrolytes and liver function tests. Baseline values may help track the progress of the condition.

Review every 2 to 3 days is likely to be adequate. However, urgent clinical review is necessary if the woman develops increasing severity of pain, increasing abdominal distension, shortness of breath and a subjective impression of reduced urine output. If the woman conceives, prolonged monitoring may be appropriate, whereas, in the absence of pregnancy, resolution would be anticipated by the time of the withdrawal bleed.

Inpatient Management

When Should Women with OHSS Be Admitted?

Women with severe OHSS require inpatient management. In addition, women with moderate OHSS who are unable to achieve control of their pain and/or nausea with oral treatment should also be admitted. Admission should also be considered where there are difficulties in ensuring adequate ongoing monitoring, until resolution commences.

Who Should Provide Care to Women With OHSS?

C - Features of critical OHSS should prompt consideration of the need for intensive care.

Women with critical OHSS require multidisciplinary care including specialists with appropriate expertise in intensive care. Specific complications, such as acute respiratory distress syndrome (ARDS), renal failure, and thromboembolism may require intensive care management. Anaesthesia and medical colleagues should be involved at an early stage in all cases of critical OHSS. Assistance should also be sought in women with severe OHSS where initial crystalloid and colloid therapy fails to correct dehydration and haemoconcentration. (Evidence level IV)

How Can the Symptoms of OHSS Be Relieved?

B - Pain relief is best provided with paracetamol and if necessary oral or parenteral opiates. Nonsteroidal anti-inflammatory agents are not recommended.

The management of OHSS is essentially supportive until the condition resolves spontaneously. Symptomatic relief is important, particularly regarding pain and nausea. Discomfort may be relieved with paracetamol or opiate medications if severe. If opiates are used, particularly in women with reduced mobility, care should be taken to avoid constipation. Nonsteroidal anti-inflammatory agents are not recommended, because they may compromise renal function in patients with OHSS. Nausea is usually related to the accumulation of ascites and so measures described to reduce abdominal distension should provide relief. Counselling

support for both the woman and her partner provides reassurance and information to allay anxiety. (Evidence level III)

How Should Women with OHSS Be Monitored?

B - Women admitted to hospital with OHSS should be assessed at least daily, with more frequent assessment of those with critical OHSS.

Assessments and measurements for inpatient monitoring of patients with OHSS are in the table below.

Table. Inpatient Monitoring of Patients with OHSS

Assessment	Measurements
History and Examination	<ul style="list-style-type: none">• Pain• Breathlessness• Hydration• Weight• Cardiovascular• Heart rate, blood pressure• Abdominal girth, distention, ascites• Intake and output chart
Investigations	<ul style="list-style-type: none">• Full blood count• Haemoglobin, haematocrit, white cell count• Urea & electrolytes• Liver function tests• Baseline clotting studies• Pelvic ultrasound (for ascites and ovarian size)• Chest x-ray or ultrasonography (if respiratory symptoms)• Electrocardiogram (ECG) and echocardiogram (if suspect pericardial effusion)

What is The Appropriate Management of Fluid Balance?

C - Allowing women to drink according to their thirst represents the most physiological approach to replacing volume.

C - Diuretics should be avoided as they deplete intravascular volume, although they may have a role with careful haemodynamic monitoring in cases where oliguria persists despite adequate intravascular volume expansion and a normal intraabdominal pressure.

Evidence to support specific regimens of fluid replacement in women with OHSS is lacking. Allowing women to drink to their thirst represents the most physiological approach to fluid volume replacement, avoiding the risk of hypervolaemia and worsening ascites that may occur with vigorous intravenous therapy. Women may need antiemetics and analgesics to enable them to tolerate oral fluid intake satisfactorily. However, where oral intake cannot be maintained, intravenous crystalloids, such as normal saline, should be used. Most women will need a fluid

intake of 2 to 3 litres in 24 hours, guided by a strict fluid balance chart. (Evidence level IV)

Women with haemoconcentration (haemoglobin greater than 14g/dL, haematocrit greater than 45%) may need more intensive initial rehydration, such as 1 litre of physiological saline over 1 hour. Women with persistent haemoconcentration and/or urine output less than 0.5 mL/kg/hour may benefit from colloids. Human albumin, 6% hydroxyethylstarch (HES), dextran, mannitol, and Haemaccel® have been used for this purpose. Few comparative data exist to support the use of any one of these over the other in the specific situation of severe OHSS. HES has been reported to be associated with a higher mean daily urine output, fewer paracenteses and shorter hospital stay than human albumin. HES is of non-biological origin and with a higher molecular weight than human albumin. If haemoconcentration and/or oliguria persist despite these measures, paracentesis should be considered. Further fluid management may be guided by central venous pressure monitoring and anaesthetists should be involved. (Evidence level III)

How Should Ascites or Effusions Be Managed?

B - Paracentesis should be considered in women who are distressed due to abdominal distension or in whom oliguria persists despite adequate volume replacement.

B - Paracentesis should be performed under ultrasound guidance to avoid inadvertent puncture of vascular ovaries distended by large luteal cysts.

B - Intravenous colloid replacement should be considered for women who have large volumes of ascitic fluid drained.

How Should the Risk of Thrombosis Be Managed?

B - Routine screening for thrombophilia in all women undergoing assisted conception is not warranted, although testing may be helpful for those with a personal or family history of thrombosis.

B - Thromboprophylaxis should be provided for all women admitted to hospital with OHSS. This should be continued at least until discharge from hospital and possibly longer, depending on other risk factors.

B - Unusual neurological symptomatology following ovarian stimulation should raise the possibility of a thrombotic episode in an uncommon location, prompting referral for appropriate expert opinion.

There are no firm data indicating either the value of diagnostic tests or heparin prophylaxis to prevent thromboembolic complications. However, as thromboembolism is a potentially life-threatening complication, prophylactic measures should be provided for all women hospitalised with OHSS, particularly with a personal or family history of thromboembolic events, thrombophilia, or vascular anomalies. Full-length venous support stockings and prophylactic heparin therapy may be used. The use of an intermittent pneumatic compression device may be helpful when symptoms prevent ambulation and confine the patient to

bed. In women who do not conceive, thromboprophylaxis may be discontinued with resolution of OHSS. The risk of thrombosis appears to persist into the first trimester of pregnancy and consideration should be given to the risks and benefits of heparin prophylaxis until the end of the first trimester, or even longer, depending on the presence of risk factors and course of the OHSS. If thromboembolism is suspected, therapeutic anticoagulation should be commenced, and additional diagnostic measures performed such as arterial blood gases, and ventilation/perfusion scan.

When is Surgical Management Indicated?

C - Pelvic surgery should be restricted to cases with adnexal torsion or co-incident problems requiring surgery and only undertaken by an experienced surgeon following careful assessment.

OHSS and Pregnancy

What are the Risks Associated With Pregnancy and OHSS?

B - Women should be reassured that pregnancy may continue normally despite OHSS, and there is no evidence of an increased risk of congenital abnormalities.

Definitions:

Grading of Recommendations

Grade A - Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)

Grade B - Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)

Grade C - Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

Levels of Evidence

Ia: Evidence obtained from meta-analyses of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well-designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study

III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Accurate diagnosis and appropriate management of ovarian hyperstimulation syndrome

POTENTIAL HARMS

- If opiates are used, particularly in women with reduced mobility, care should be taken to avoid constipation.
- Diuretics may worsen intravascular dehydration
- Complications of paracentesis, including risk of puncture of vascular ovaries and cardiovascular collapse from massive fluid shifts

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines are "systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions." Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1: Guidance for the Development of RCOG Green-top Guidelines (See the "Availability of Companion Documents" field in this summary.)
- These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice.

Attention is drawn to areas of clinical uncertainty where further research may be indicated.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Royal College of Obstetricians and Gynaecologists (RCOG). The management of ovarian hyperstimulation syndrome. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2006 Sep. 11 p. (Green-top guideline; no. 5). [34 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1995 Jan (revised 2006 Sept)

GUIDELINE DEVELOPER(S)

Royal College of Obstetricians and Gynaecologists - Medical Specialty Society

SOURCE(S) OF FUNDING

Royal College of Obstetricians and Gynaecologists

GUIDELINE COMMITTEE

Guidelines and Audit Committee of the Royal College of Obstetricians and Gynaecologists

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Mr JM Jenkins, FRCOG, Bristol; Mr AJ Drakeley, MRCOG, Liverpool; and Dr RS Mathur, MRCOG, Cambridge

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Guideline authors are required to complete a "declaration of interests" form.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Royal College of Obstetricians and Gynaecologists (RCOG). Management and prevention of ovarian hyperstimulation syndrome. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2005 Jan.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Royal College of Obstetricians and Gynaecologists \(RCOG\) Web site](#).

Print copies: Available from the Royal College of Obstetricians and Gynaecologists (RCOG) Bookshop, 27 Sussex Place, Regent's Park, London NW1 4RG; Telephone: +44 020 7772 6276; Fax, +44 020 7772 5991; e-mail: bookshop@rcog.org.uk. A listing and order form are available from the [RCOG Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Development of RCOG green-top guidelines: policies and processes. Clinical Governance Advice No 1a. 2006 Nov. Available from the [Royal College of Obstetricians and Gynaecologists \(RCOG\) Web site](#).
- Development of RCOG green-top guidelines: producing a scope. Clinical Governance Advice No 1b. 2006 Nov. Available from the [Royal College of Obstetricians and Gynaecologists \(RCOG\) Web site](#).
- Development of RCOG green-top guidelines: producing a clinical practice guideline. Clinical Governance Advice No 1c. 2006 Nov. Available from the [Royal College of Obstetricians and Gynaecologists \(RCOG\) Web site](#).

- Searching for evidence. Clinical Governance Advice No 3. 2001 Oct. Available from the [Royal College of Obstetricians and Gynaecologists \(RCOG\) Web site](#).

Additionally, auditable standards can be found in section 11 of the [original guideline document](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on November 30, 2007. This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection.

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